

# HD 101

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# Presenter Disclosures

Holly Shill

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose  
or list

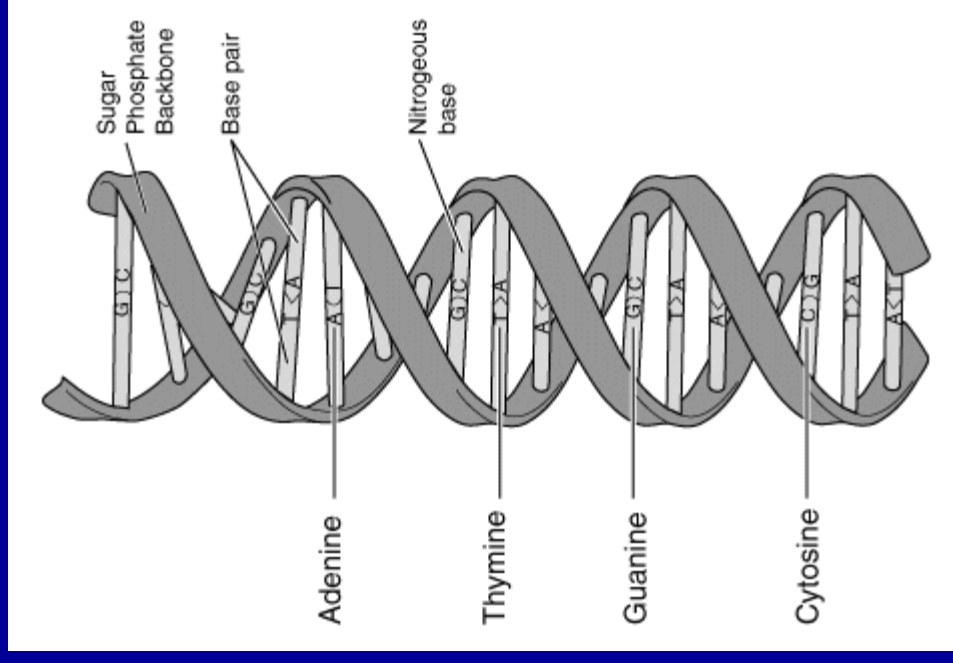
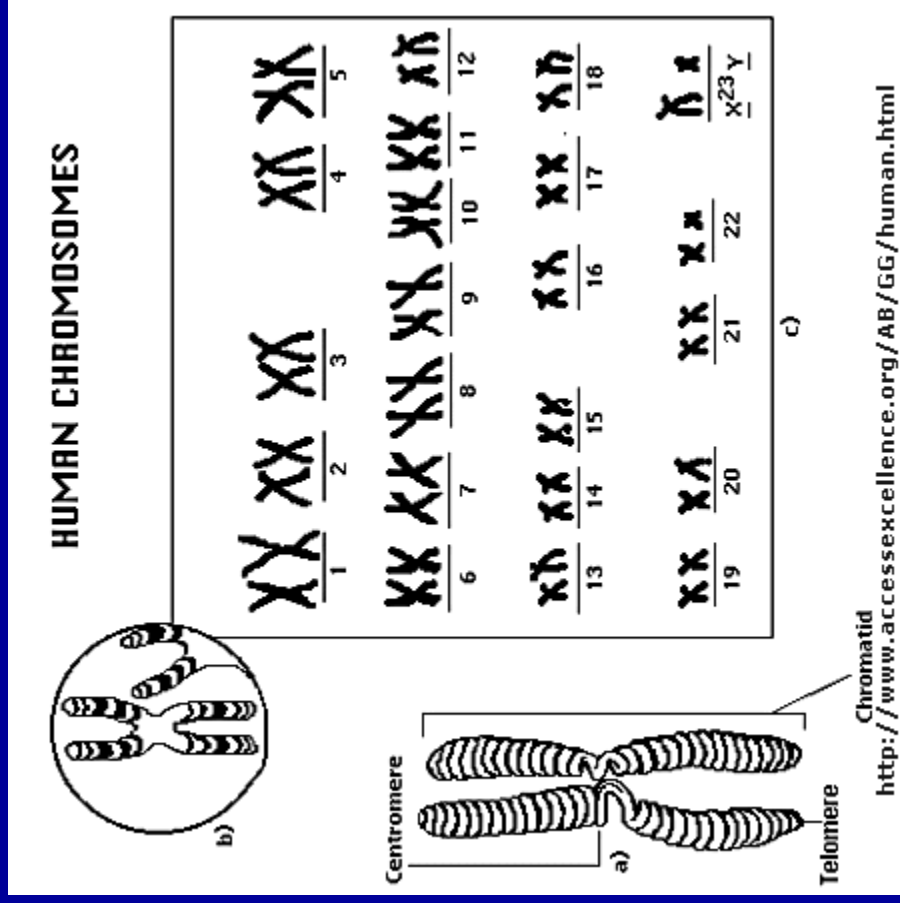


**Huntington's Disease Society of America**

# History

- 1872- “On Chorea” by George Huntington
  - clinical symptoms
  - hereditary nature of the disease
- 1955- Lake Maracaibo, Venezuela
  - Americo Negrette
- 1967- Woody Guthrie dies of HD
  - HD SA
- 1981- Wexler begins field work in Venezuela
- 1983- Gene located - chromosome 4p16.3

# Genetics



# Genetics

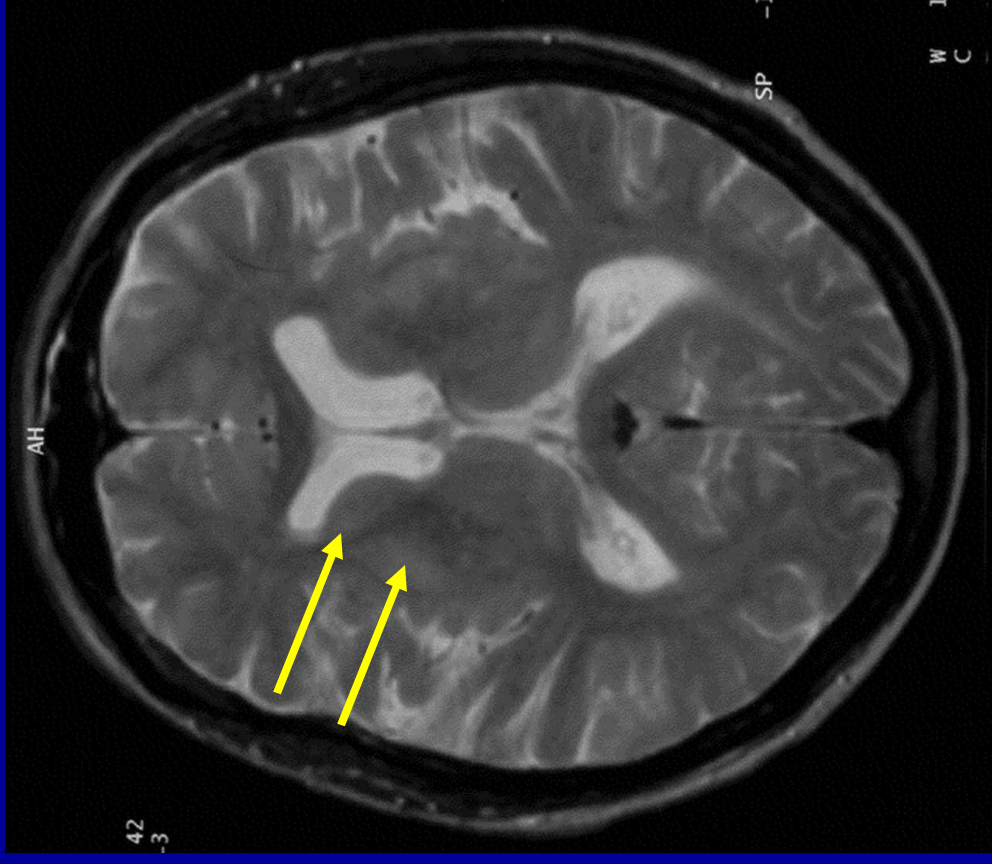
- Autosomal dominant
- Each child has 50% chance inheritance
- CAG repeat or expansion
- Excessive glutamine in Huntington protein
- Normal CAG 10-35
- Borderline CAG 27-35
  - may expand if passed by male
- Low abnormal CAG 35-39
  - may develop disease
- Abnormal CAG >40
  - will develop disease

# Other genetic concepts

- CAG repeats correlate with age of onset
- CAG repeats may expand
  - Paternal transmission
- Absent family history
  - 2-5%
    - Non-paternity, new mutation
- Diagnostic testing
  - Patient has symptoms
- Predictive testing
  - AHSC, Tucson

# Pathology

- Basal ganglia
  - Caudate>putamen
- Loss of GABA
- Increases in dopamine/adrenalin
- NMDA increased “excitotoxicity”
- Mitochondrial inhibitors (3-NP)
  - Animal model





# Course and Prognosis

- Average age onset = 40 years
  - 10% <20, 10% >60
- Average survival 15-20 years although varies
- Initially, mood changes and subtle cognitive issues
- Chorea more prominent in middle stages
- Advanced stages with dementia and parkinsonism

# Clinical Features

- Motor symptoms
- Cognitive symptoms
- Behavioral symptoms
- Psychiatric symptoms

# Chorea

- Restlessness
- “piano playing” fingers; “milkmaid’s grip”
- Can be suppressed
- Increased with stress or paying attention
- Ranges from not interfering to incapable of walking, speaking or eating

# Chorea

- Treatment:
  - When socially or physically disabling
- Medications:
  - Dopamine reuptake inhibitors (tetraabenazine)
  - Dopamine blocking drugs (haloperidol)
  - Muscle relaxants (diazepam)

# Incoordination

- Motor sequencing- fine motor
- Bradykinesia- slow movements
- Dysarthria/Dysphagia- speech/swallow
- Gait instability and falls
- Leading cause of nursing home placement
- More difficult to treat
  - PT/OT/ST

# Cognition

- Subcortical dementia
- Different from Alzheimer's disease (cortical)
- Testable by neuropsychological tests of memory, language ability, visual spatial skills, attention and concentration, and judgment

Ability	Huntington's Disease	Alzheimer Disease
<i>Speed of processing</i>	Slow, but relatively accurate	Slow, often inaccurate
<i>Speech output</i>	Slurred and slow, but accurate	Normal in clarity and rate; often the incorrect word
<i>Learning new information</i>	Disorganized and slow, but can learn	Rapid forgetting, defective storage of information
<i>Free recall of memory</i>	Impaired: cannot find the right word;...can recognize with choices, benefits from cues	Impaired: memory store is defective; ....cannot recognize, cues don't help
<i>Motor memory</i>	Impaired: cannot learn or recall motor memories	Intact: can learn and retain motor memories

# Personality

- Suspicious
- Aggression /Irritable
- Eccentric
- Untidy
- Excessively religious
- False sense of superiority
- Impulsive
- Sedentary



# Behavior

- Outbursts of temper
  - Hunger, thirst, pain, inability to communicate, frustration with failing abilities, boredom, changes in routine
- Fits of despondency
- Jealousy
- Sexual promiscuity/Paraphilias
  - (voyeurism, exhibitionism)
- Alcoholism
  - 17% in males
  - 6% in females
- Smoking
  - Cardiovascular mortality high

# Behavior

- Divorce
  - No good studies
  - Experience suggests it is more common
- Decreased ability to manage household
- Work performance
- Jail
- Total functional capacity (work, home, self-care)

# Psychiatric issues

- Mood disturbances
  - Depression
  - Anxiety
  - Mania
- OCD
  - Mild obsessiveness can be seen
- Psychosis
  - Hallucination rare
  - Delusion more common but still rare

# Depression

- Depression
  - Studies suggest about 40%
  - 22 % of the 40 % meet criteria for MD
  - Not correlated with disease severity
  - Can predate HD by years in “at risk” population but can occur at any stage of the disease
  - Apathy in NOT depression
  - Treat if necessary
  - Suicidal attempt-7.3%-12%,
    - greater than average risk

# Anxiety/OCD

- Anxiety
  - Excessive worry
  - Irritability
  - Poor sleep
  - Can respond to treatment
- OCD
  - SSRIs
  - Psychotherapy is difficult

# Mania

- Small number of patients 4.8-10%
- Presents with
  - Elevated or irritable mood
  - Grandiosity
  - Impulsivity
- May be confused with bipolar illness
- Treatment: Avoid lithium, use valproate or carbamazepine

# Disease modification

- Studied, not helpful
  - Remacemide
  - Riluzole
  - Ethyl-EPA
- Still of interest
  - Creatine
  - CoQ10
- Promising?
  - Stem cells
  - Antidepressants, tiagabine, rosaglitazone
  - Specific mitochondrial agents

# Living with HD

- Address genetic issues
  - Family planning, discrimination
- Address social issues
  - Disability, living arrangements, EOL, POA
- Address neuropsychiatric issues
- Address mobility aspects
- Participate in research
- Local support groups/community outreach
- Quality of life!



# Thanks!

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